PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	04.02.2005
Applicant's or agent's file reference: PU5025WO/KLP	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/35830	07.11.2003	08.11.2002

Applicant: GLAXO GROUP LIMITED et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PU5025WO/KLP		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/35830	07.11.2003	08.11.2002
International Patent Classification (IPC) or both national classification and IPC		
A61K9/00		
Applicant		
GLAXO GROUP LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05.05.2004	04.02.2005
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Scarponi, U Telephone No. +31 70 340-3292

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/35830

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-17 as originally filed

Claims, Numbers

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 14

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 14

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Present claim 14 relate to subject-matter considered by this Authority to be covered by the provisions of **Rule 67.1 (iv) PCT**. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (**Article 34 (4) (a) (i) PCT**).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US-A-5 681 581 (J.M.DUNN) 28 October 1997 (1997-10-28);

D2: US-A-4 917 900 (H.P.JONES ET AL.) 17 April 1990 (1990-04-17);

D3: WO 98/18477 A (GLAXO) 7 May 1998 (1998-05-07);

D4: US-B-6 177 4351 (B.A.LARDER ET AL.) 23 January 2001 (2001-01-23) (equivalent to **WO9323021 [THE WELLCOME FOUNDATION LTD.,UK] 25 November 1993 [1993-11-25]).**

V.1. Present **independent claims 1 and 2** do not meet the requirements of **Article 6 PCT** in that the matter for which protection is sought is not clearly defined. In fact the terms ***"pharmaceutically acceptable derivative thereof "*** used in said claims are vague and unclear and leave the reader in doubt as to the meaning of the technical feature/s to which they refer, thereby rendering the definition of the subject-matter of said claims unclear, **Article 6 PCT.**

V.2. For the assessment of the **present claim 14** on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.3. The present application does meet the criteria of **Article 33(1) PCT**, because the subject-matter of **present claims 1-14** is new in the sense of **Article 33(2) PCT**.
In fact, the **document D4**, which is considered to represent the most relevant state of the art, discloses (the references in parentheses applying to this document) **compositions comprised of a combination of zidovudine and lamivudine, some of said compositions being described as controlled-release compositions containing a hydrogel polymer such as HPMC** (see in particular the examples of document D4).
Therefore the subject-matter of **present independent claims 1 and 2** differs from the teachings of document D4 in that **a formulation of a combination of zidovudine and lamivudine should be associated with a controlled-release formulation of zidovudine in the inventive (layered) composition.**
The subject-matter of **present claims 1-14** is therefore new **(Article 33(2) PCT).**

V.4. On the other hand, the above mentioned **document D4** can be regarded as being the closest prior art to the subject-matter of **present claims 1-14**.
The **problem** to be solved by the present invention (see the description of the present Application, page 2, lines 18-27; page 5, line 21 to page 6, line 3; page 13, lines 13-19) may in fact be regarded as **to overcome the problems and the drawbacks connected with a unitary-dose combination composition of the two actives (zidovudine and lamivudine)** such as the compositions of document D4 (and of document D3 as well).
The solution to this problem proposed in present claims 1-14 of the Application is considered as involving an inventive step **(Article 33(3) PCT)** because **the association of a unitary-dose combination formulation of the two actives (zidovudine and lamivudine) with a controlled-release formulation of zidovudine in a single (layered) composition suitable for once-daily administration can in the same time overcome patient-compliance problems and guarantee the desired release kinetics of the active agent(s).**
Therefore, the present Application does meet the criteria of **Article 33(1) PCT**, because the subject-matter of **present claims 1-14** does involve an inventive step in the sense of **Article 33(3) PCT.**